Current Status of Provocative Food Testing

PROVOCATIVE FOOD TESTING was revived and popularized by Rinkel and Lee in 1960, and the technique has had numerous proponents since that time. The method, however, remains controversial and is not generally used in the diagnosis of food (or other) allergy by most allergists. The testing procedure consists of the intradermal injection of a food extract of potency and volume sufficient to induce systemic symptoms, followed by the immediate injection of a small amount of the same food extract to neutralize the symptoms. Duke, in 1921, described a similar procedure in which food extracts were used to produce symptoms in patients with gastrointestinal and genitourinary complaints followed by neutralization of the symptoms with epinephrine. A recent modification of this procedure utilizes sublingual administration of food extracts or other materials. Advocates of these methods claim an accuracy of up to 85 percent in identifying specific food sensitivity. Such advocates also state it is imperative that the patient have complete evaluation of inhalant allergy to pollens, dust, molds, and epidermals, and that environmental allergen control is essential before food testing.

Long overdue objective scientific evaluation of these provocative-neutralizing techniques is now being performed. The validity of the technique was not established in one recent study of 20 patients with food allergy.

BEN C. EISENBERG, MD

REFERENCES

Dickey LD: Ecologic illness—Investigation by provocative tests with foods and chemicals. Rocky Mt Med J 68:23-28, Oct 1971

Bronsky EA, Burkley DP, Ellis EF: Evaluation of the provocative food test technique. J Allerg 47:104, Feb 1971

Inhibition of Histamine Release by Cyclic 3', 5'-Adenosine Monophosphate (CAMP)

THERE IS MUCH REASON to believe that exposure to antigen produces allergic symptoms, such as asthma and allergic rhinitis, by stimulating the release of histamine and slow reacting substance of anaphylaxis (SRS-A) from IgE-sensitized blood basophiles or tissue mast cells at the target or shock organ sites.

In examining the mechanism involved in the antigenic release of histamine and SRS-A, it has been learned that materials such as isoproterenol, theophylline, dibutyryl CAMP, and prostaglandins E_1 and E_2 which mimic or increase the cellular content of CAMP also inhibit the release of histamine and SRS-A from human lung tissue or leukocytes. Other leukocytic functions, such as the killing of target cells by lymphocytes and lymphocytic transformation, are also inhibited by these materials.

In the many cellular systems in which CAMP has been studied, it usually functions as a "second messenger" to promote a hormone-induced *stimulating* action. The *inhibition* of allergic histamine release by CAMP stands as an interesting contrast.

Further studies of the histamine release mechanism, however, are clearly needed since other materials such as cholinergic agents disodium cromoglycate and diethylcarbamazine, which also inhibit allergic histamine release, apparently have no influence on cellular CAMP levels.

GILDON N. BEALL, MD

REFERENCES

Bourne HR, Lichtenstein LM, Melmon KL: Pharmacologic control of allergic histamine release *in vitro:* Evidence for an inhibitory role of 3', 5'-adenosine monophosphate in human leukocytes. J Immunol 108:695-705, Mar 1972

Orange RP, Austen WG, Austen KF: Immunological release of histamine and slow-reacting substance of anaphylaxis from human lung. I. Modulation by agents influencing cellular levels of cyclic 3', 5'-adenosine monophosphate. J Exp Med 134:(Supplement) 136-148, Sep 1971

Status of Testing for Penicillin Allergy

ANAPHYLAXIS and other allergic reactions continue to be a major concern to all those administering and receiving penicillin therapy. Skin tests with penicillin G and several of its derivatives appear to be the simplest and most practical way to predict allergic reactions to penicillin. The major antigenic determinant derived from penicillin G is penicillenic acid which, through the penicilloyl (BPO) radical complexed to body protein, acts as a sensitizing antigen for the stimulation of antibody production. IgE anti-BPO antibodies are thought to be responsible for penicillin-induced urticaria and reactions of serum sickness type. Penicilloyl polylysine (BPO-PPL) skin tests detect these IgE antibodies, while BPO-PPL hemagglutination tests detect IgM and IgG antibodies. Minor antigenic determinants derived from penicillin G, including penicillenate, penamaldate, penicillamine and penicillin G itself can induce IgE antibodies important as causes of anaphylactic reactions. These IgE antibodies may be detected by skin tests with a minor determinant mixture (MDM). Clinical studies have demonstrated that

only 14 to 27 percent of patients with a history of penicillin allergy may actually have IgE antibodies. In patients with negative skin tests with both BPO-PPL and MDM, penicillin administration has not caused immediate or accelerated allergic reactions. Since neither MDM nor BPO-PPL are commercially available, routine skin testing is still not possible. Until these reagents become available, clinicians must rely on the patient's history despite its fallibility.

O. L. FRICK, MD

REFERENCES

DeWeck AL: Immunochemical mechanisms of hypersensitivity to antibiotics. *In* Serafini U(Ed): New Concepts in Allergy and Clinical Immunology. Amsterdam, Excerpta Medica, 1971, p. 208

Levine BB, Zolov DM: Prediction of penicillin allergy by immunological tests. J Allerg 43:231-244, Apr 1969

Adkinson NF Jr, Thompson WL, Maddrey WC, et al: Routine use of penicillin skin testing on an in-patient service. N Engl J Med 285:22, Jul 1971

Bronchiolitis—A Stage of Incipient Bronchial Asthma?

BRONCHIOLITIS is an important cause of acute lower respiratory tract disease in infants. Hall marks of the disease include: (1) an acute onset of respiratory distress with sibilant rales and wheezes, (2) evidence of obstructive pulmonary hyperinflation clinically and by radiologic examination, (3) normal temperature or low-grade fever, (4) absence of past history of wheezing. A viral infection, particularly respiratory syncytial virus, is thought to be the most important cause. Differentiation from bronchial asthma is not easy, since bronchial smooth muscle responsiveness to bronchodilators is not good in this age group. Retrospective studies have suggested that in 30 to 50 percent of children with bronchiolitis, bronchial asthma develops later in childhood.

Two recent prospective studies revealed that 50 percent of these children, when followed five to eight years after the initial episode, had recurrent wheezing. Important prognostic indicators include: (1) positive family history of atopy, (2) other allergic manifestations (for example, hay fever, atopic dermatitis), (3) nasal eosinophilia, and (4) significantly positive reaction to skin tests with common inhalant allergens. It is postulated that patients with an atopic diathesis are more likely to have wheezing with a viral respiratory infection. However, further epidemiological work on the effects of respiratory viral infections on the non-atopic patients is needed to confirm this impression.

These studies strongly suggest that bronchiolitis is frequently followed by asthma, particularly in infants with other markers of the atopic state. Prophylactic measures aimed at lessening allergenic exposure at this critical period should be evaluated to determine whether the prognosis can be altered.

STANLEY P. GALANT, MD

REFERENCES

Phelan PD: Studies of respiratory function in infants with recurrent asthmatic bronchitis. Aust Paediat J 5:187-196, Dec 1969

Zweeiman B: Patterns of allergic respiratory distress in children with a past history of bronchiolitis. J Allerg 48:283-289, Nov 1971

Rooney JC: The relationship between proved viral bronchiolitis and subsequent wheezing. J Pediat 79:744-747, Nov 1971

Pitfalls in the Use of Skin Testing in Allergy

TWO RECENT REPORTS deal with some of the pitfalls in allergy skin testing. One of these reemphasizes what has been known for some time but is often lost sight of—that positive skin tests alone do not reflect active clinical allergy. Whitcomb tested 50 medical students, taken at random, for sensitivity to nine inhalants and eight food allergens. Almost two-thirds of them (32) had positive reactions (two plus or more). In all there were 100 such positive reactions, 84 to inhalants and 16 to foods. No one reacted to food tests alone. Only about half (17) of the 32 who had positive tests had experienced clinical symptoms in the preceding year. The discovery of positive reactions came as a surprise to the other half. It would seem that either their challenge with the antigens concerned was insufficient or some other factor in the allergic response was missing.

Allergists have differed in their opinion about the extent to which drugs used in treatment of allergic disease affect skin tests. The matter has recently been reinvestigated. Hydroxyzine, (Atarax®, Vistaril®), diphenhydramine (Benadryl®) and chlorpheniramine (Chlor-Trimeton®, Teldrin®) produced significant skin test inhibition. The effect of hydroxyzine was profound at one hour after drug administration and was still present at 24 hours. Ephedrine, aminophylline and prednisone had no effect on the skin tests. It is concluded that antihistamines and hydroxyzine should be discontinued for at least 24 hours before skin testing.

WILLIAM C. DEAMER, MD

REFERENCES

Whitcomb N: Incidence of positive skin tests among medical students. Ann Allerg 29:67-70 Feb 1971

Galant S, Zippin C, Bullock J, et al: Allergy skin test: Antihistamine inhibition. Ann Allerg 30:53-61, Feb 1972

Wolfe, HL, Fontana UL: The effect of tranquilizers on immediate skin wheal reaction. J Allerg 35:271-273, May-Jun 1964